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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/746,635	11/13/96	MURTHY	V 96700/341

EXAMINER	
SPIEGEL, C	
ART UNIT	**PAPER NUMBER**
1817	8

18M1/0519

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NEW YORK NY 10016

DATE MAILED: 05/19/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-4, 8-10, 13-15 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-4, 8-10, 13-15 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1996-404-498/40517

CHANGE IN ART UNIT

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1817**.

REFERENCE TO PARENT REQUIRED IN 37 CFR § 1.62 APPLICATION

This application filed under 37 C.F.R. § 1.62 lacks the necessary reference to the prior application. A statement reading "This is a CONTINUATION of application Serial No. 08/421,079, filed April 13, 1995" should be entered following the title of the invention or as the first sentence of the specification. Also, the present status of the parent application(s) should be included.

CLAIM STATUS

Claims 1, 2, 4, 8, 9 and 13-15 were amended in the response filed January 2, 1996 (paper #4) which response also cancelled claims 5-7, 11-12 and 16-18. Thus, claims 1-4, 8-10 and 13-15 are pending.

DRAWINGS

The drawings are objected to for reasons of record (see PTO-948 attached to paper #3). Correction is required.

NON-ART BASED REJECTIONS

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written descrption of the invention.

The peaks on Figure 2 are not labelled. Applicant is cautioned against introducing new matter when making changes involving the drawings. Proposed drawing correction and/or the proposed substitute sheets of drawings must be embodied in a separate letter and show such changes in red ink (see page 142, Murthy, *Journal of Clinical Laboratory Analysis*, 8:140-143 (1994) where the peaks are labelled).

Claims 13-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 appears incomplete because the calculating step appears to require some means of either determining erythrocyte adenylate kinase concentration/activity *per se* or differentially measuring what part of the total detection signal is attributable to *erythrocyte* adenylate kinase.

Claim 15, step d) is confusing because measurement of total fluorescence emission indicates total detection signal, not the total adenylate kinase activity/concentration, without correlation to a known standard. Similarly, the calculation in step f) appears based upon relative fluorescence emissions rather than relative enzyme concentrations. Finally, --the--

should be inserted before "total" in line 13 for consistent language. In the alternative, the claims should refer to "total" activity versus "the/said total activity" when initially recited.

ART BASED REJECTIONS

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, ~~13~~ and ~~14~~ are rejected under 35 U.S.C. § 103(a) as being unpatentable over Olsson et al. (*Journal of Applied Biochemistry*, 5: 437-445 (1983)).

Claims 2, 3 and 15/17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Olsson et al. (*Journal of Applied Biochemistry*, 5: 437-445 (1983)) as applied to claims 1 and 13 above, and further in view of Tsuji et al. (Chemical Abstract 86:39099)) or Friedrich et al.

(*Biochemical Genetics*, 22 (5/6): 389-394 (1984)) and, if necessary, further in view of Buth et al. (Biological Abstract 71059076 (1981)).

Claims 4 and 8-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Olsson et al. (*Journal of Applied Biochemistry*, 5: 437-445 (1983)) as applied to claims 1 and 13 above, and further in view of Matsuura et al. (*Journal of Biological Chemistry*, 264 (17): 10148-10155 (1989)).

The claimed invention is directed to (1) detection of hemolysis and/or conditions producing hemolysis by measuring serum adenylate kinase: and, (2) determination of serum erythrocyte adenylate kinase activity.

Olsson et al. found that (i) adenylate kinase was concommitantly released with hemoglobin during cell aging; (ii) cell aging results in progressive lysis of erythrocytes; (iii) adenylate kinase was suitable for monitoring cell lysis due to its extreme storage stability; (iv) there was a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase; and, (v) while hemolysis was conventionally measured by measurement of extracellular hemoglobin, adenylate kinase activity measurement was also a sensitive and convenient way to follow hemolysis. An advantage of measuring adenylate kinase lies in studying the lysis of other cell types, e.g. platelets (see page 437; Table I; page 445). Olsson et al. determined adenylate kinase activity in plasma by measuring formation of ATP from ADP by the firefly luciferase reaction. DAPP, which is a specific inhibitor of erythrocyte adenylate kinase, confirmed the origin of the adenylated kinase in the plasma to be erythrocytic (page 442). Thus, Olsson et al. differ is detecting hemolysis by determining

erythrocyte adenylate kinase activity in plasma rather than in serum. However, it would have been obvious to one of ordinary skill in the art to modify the method of Olsson et al. by determining erythrocyte adenylate kinase activity in serum rather than plasma because serum and plasma are conventional alternative samples used in clinical analysis derived from whole blood.

Olsson et al. also differ in failing to disclose alternative methods for determining erythrocyte adenylate kinase activity, e.g. including the use of gel electrophoresis and immunochemistry, which differentiate adenylate kinase activity of erythrocytic origin from adenylate kinase activity from other cells. Tsuji et al. measure erythrocyte adenylate kinase by agarose thin-layer gel electrophoresis with tetrazolium (i.e.formazan) visualization. Friedrich et al. describe electrophoretic separation and visualization of human erythrocyte adenylate kinase. Buth et al. use NAD-dependent glucose-6-phosphate dehydrogenase in adenylate kinase enzyme staining/detection procedures because it is significantly less expensive than utilizing NADP. Matsurra et al. describe immunoblot analysis of human erythrocyte adenylate kinase (AK1). Thus, it would have been further obvious and well within ordinary skill in the art to measure erythrocyte adenylate kinase by any known and conventional assay therefore, including electrophoretic separation and staining, such as with NAD-dependent glucose-6-phosphate dehydrogenase visualization technique, immunoassays, etc. as suggested by Tsuji et al., Friedrich et al., Buth et al. and/or Matsurra et al.

FIRST ACTION FINAL

This is a CONTINUATION of applicant's earlier application S.N. 08/421,079. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds or art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See M.P.E.P. § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

CLOSING

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carol A. Spiegel whose telephone number is (703) 308-3986.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Carol A. Spiegel
May 16, 1997

Carol A. Spiegel

CAROL A. SPIEGEL
PRIMARY EXAMINER
GROUP 1800